REMARKS/ARGUMENTS

This is in response to the office action dated January 11, 2005. Claims 2-5, 8, 9, 12 and 17-19 are pending in the application. Claims 2 and 17-19 are rejected. Claims 3-5, 8 and 9 are objected to. Claim 12 is withdrawn from consideration and claim 19 has been canceled.

Claims 2 and 17-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner has requested that in main claim 2 it should be made clear that the last "Z" choice only applies to the last choice in "L" consistent with the specification and the resulting spiro fusion. By the present amendment claim 2 has been amended by having the proviso clearly reflect the definition of "Z" in relation to "L". It is believed that the claims as amended are consistent with the disclosure.

The Examiner has requested that "in the definition of B_1/B_2 forming a 5 or 6-membered carbocyclic ring it should be made clear that B_1 and/or B_2 are methylene" in order to form the claimed five or six-membered ring. By the present amendment claim 2 has been amended to reflect that B_1 and/or B_2 are methylene.

Claims 18 and 19 are deemed to be substantial duplicates of each other. By the present amendment claim 19 has been canceled and claim 18 has been amended by the inclusion of the specific diseases and disorders associated with the NPY Y5 receptor subtype which were originally in claim 19.

Claim 17 is deemed to be of indeterminate scope in that the diseases are defined by their underlying cause which is deemed to render the scope of the intended uses indeterminate. By the present amendment claim 17 has been amended by the inclusion of the specific diseases and disorders associated with the NPY Y5 receptor subtype.

Claim 17 is rejected under 35 U.S.C. 112, first paragraph, on the ground that the specification, while being enabling for treating obesity, does not reasonably provide enablement for the remaining uses covered by claim 17. The Examiner has concluded further that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with the claims.

Endogenous receptor proteins that bind NPY and related peptides as ligands have been identified and distinguished and several such proteins have been cloned and expressed. Six different receptor subtypes [Y1, Y2, Y3, Y4 (PP), Y5, Y6 (formerly designated as a Y5 receptor)] are recognized today based upon binding profile, pharmacology and/or composition, if identity is known. (*Wahlestedt, C. et al., Ann. NY Acad, Sci., 1990, 6117*) Neuropeptide Y is the archetypical substrate for the NPY receptors and its binding can elicit a variety of pharmacological and biological effects *in*

vitro and *in vivo*. For example, when administered to the brain of live animals (intracerebroventricularly (icv) or into the amygdala), NPY produces anxiolytic effects in established animal models of anxiety such as the elevated plus-maze, Vogel punished drinking and Geller-Seifter's bar-pressing conflict paradigms. Thus compounds that mimic NPY are postulated to be useful for the treatment of anxiolytic disorders (*Heilig, M. et al. Neuropsycho-pharmacology 1993, 8, 357*).

The immunoreactivity of neuropeptide Y is notably decreased in the cerebrospinal fluid of patients with major depression and those of suicide victims (*Widdowson, P.S. et al., Journal of Neurochemistry, 1992, 59, 73*). Rats treated with tricyclic antidepressants display significant increases of NPY relative to a control group (*Heilig, M. et al. European Journal of Pharmacology 1988, 147, 465*).

Neuropeptide Y improves memory and performance scores in animal models of learning (*Flood, J.F. et al., Brain Research 1987, 421, 280*) and therefore serves as a cognition enhancer for treatment of neurodegenerative diseases such as Alzheimer's Disease as well as AIDS-related and senile dementia.

Neuropeptide Y also mediataes endocrine functions such as the release of luteinizing hormone (LH) in rodents (*Kalra, S. P. et al. Frontiers in Neuroendocrinology 1992, 13, 1*). Since LH is vital for mammalian ovulation, a compound that mimics the action of NPY could be useful for the treatment of infertility, particularly in women with so-called luteal phase defects.

The Kehne *et al.* reference cited by the Examiner is a chapter in Annual Reports In Medicinal Chemistry. The Table referred to by the Examiner (Table I) is not the current state of the art related to NPY 5 antagonists as indicated by the Examiner. The Table contains a list of antagonists for NK, CRF, NPY and MCH receptors and a therapeutic indication for each receptor. There is nothing in the Table that would indicate that the stated indication for each antagonist receptor is the only indication for that receptor. On page 12 of that chapter there is a discussion of the role of NPY Receptor Antagonists in the treatment of obesity. There is no discussion in the Chapter of other uses or the lack thereof for the NPY Y5 receptor.

Applicants also wish to point out that WO98/35957 describes amide derivatives that are NPY Y5 receptor antagonists which are used to treat NPY mediated disorders including eating disorders such as bulimia and obesity related disorders including type II diabetes, hypertension, memory disorders, and related disorders such as epilepsy and depression, among others.

WO97/19682 describes aryl sulfonamide and sulfamide derivatives which inhibit the activity of the human Y5 receptor and as such are useful for the treatment of, for example, obesity, anorexia nervosa, bulimia nervosa, abnormal conditions such as sexual/reproductive disorders, depression, epileptic seizures, sleep disturbances etc.

The present application is a division of application Serial No. 09/626,856, now U.S. patent No. 6,380,224. The '224 patent issued with broad method of treatment and pharmaceutical composition claims for the treatment of disorders or disease states caused by eating disorders, obesity, bulimia nervosa, diabetes, memory loss, epileptic seizures, migraine, sleep disturbances, pain, sexual/reproductive disorders, depression and anxiety. Although the presently claimed compounds were not claimed in the issued patent they were disclosed in the patent as having the utility claimed in the issued patent. Having allowed the broad method of treatment claims in the parent application, it is submitted that the same scope should be awarded to the compounds making up the divisional application.

Applicants have submitted a list of publications, including patents issued by the USPTO, which indicate that the Y5 receptor has multiple uses. This being the case, one skilled in the art, given the disclosures in the prior art relating to the Y5 receptor, would have a reasonable expectation of success in treating the diseases claimed in the present application. It is generally accepted that, in pharmaceutical cases, *in vitro* as well as *in vivo* data are acceptable for purposes of patentability.

Applicants submit that the prior art clearly demonstrates that compounds which are ligands for the neuropeptide NPY Y5 receptor have multiple uses. All that the courts require is a reasonable correlation between the activity and the asserted uses, Nelson v. Bowler, 626 F. 2d., 853, 857.

Reconsideration of the rejection of claim 17 under 35 U.S.C. 112 is courteously requested.

Claims 2 and 17-19 are rejected under 35 USC 112, first paragraph, for failing to comply with the written description requirement in that the claims are believed to contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors at the time the application was filed, had possession of the claimed invention. The Examiner has pointed out that the present proviso appears to permit other "Z" choices for the elected piperidino "L"link which were excluded in the disclosure as originally filed. As support for the rejection the Examiner has directed applicant's attention to the disclosure at the top of page 12 of the specification. By the present amendment the proviso in claim 17 has been amended to conform to the language disclosed in the specification on page 12. It is believed that the claim as amended limits the proviso to that which was originally disclosed.

Reconsideration of the rejection of claims 2 and 17-19 under 35 U.S.C. 112 is courteously requested.

Claims 2 and 17-19 are rejected under 35 USC 102(b) as being anticipated by Youngman which describes a compound believed to be within the elected scope for uses based on NPY 5 antagonistic activity. Although the publication date of the reference is later than the filing date of the instant application, the Examiner maintains that Youngman is a valid reference because applicants are only accorded the instant filing

date in view of the lack of compliance with 35 USC 112, paragraph one, for the reasons set forth in the 112 rejection. Applicants submit that Youngman would be a valid reference only if applicants were unable to overcome one or more of the 112 rejections. In view of the above discussion and the amendments made to the claims in this amendment, it is believed that all of the 112 rejections have been removed. Therefore, Youngman is not a valid reference against the present claims since its publication date is later than the effective filing date of the present application.

Reconsideration of the rejection of claim 2 and 17-19 under 35 U.S.C. 102(b) is courteously requested.

Claims 3-5, 8 and 9 remain objected to as being dependent upon a rejected base claim. Applicants have not written claims 3-5, 8 and 9 in independent form, as proposed by the Examiner, because it is believed that all of the outstanding rejections have been removed.

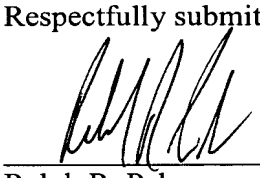
Applicants note that EP'555 was only cited to show the status of the art. Since no claims stand rejected over the reference, a detailed discussion of the reference is not deemed necessary.

Applicants acknowledge receipt of the 2nd page of the signed copy of the IDS filed on 12/17/03, which had not been signed by the previous Examiner.

In view of the above discussion and the amendments herein being made to the claims, it is believed that all of the outstanding objections and rejections have been removed.

Applicants respectfully request that a timely Notice of Allowance be issued in this application.

Respectfully submitted,



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